REMARKS

Applicant acknowledges that the priority foreign applications to Korean Patent 10-2002-0015708 have been received and have been placed in the record.

The rejection of claim 3 under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is respectfully traversed.

Applicant has amended claim 3 to correct the recitation deemed to be indefinite by the Examiner. Claim 3 now reads "murine monoclonal antibody variable regions that bind hepatitis B virus pre-S1 antigen", as suggested by the Examiner. Accordingly, the rejection of claim 3 under 35 USC 112, second paragraph should be withdrawn.

The rejection of claims 6, 7 and 10 under 35 USC 112, first paragraph, as failing to comply with the enablement requirement is respectfully traversed.

The Examiner alleges that the biological Deposit of the hybridoma cell lines producing antibodies DP-JH4 and DPH12-JK4, the specified sequences for the human antibody heavy DP-JH4 and light chain DPH12-JK4, and the plasmids carrying the said sequences have not been adequately described in the present specification or in the sequence listing, and therefore the specification does not adequately teach how to make and use the claimed invention.

However, Tomlinson et al (J. Mol. Biol., 227, 776-798, (1992) and Ravetch et al (Cell, 27, 528-519 (1981) disclose that DP7 is human immunoglobulin germline VH (V_H) gene segment and JH4 (J_H4) is human germline segment. Also, Cox et al (Eur. J. Immunol., 24, 827-836 (1994) and Hieter et al (J. Biol. Chem., 257, 1516-1522 (1982) disclose that DPK 12 is human immunoglobulin germline VK (V_K gene segment and JK (J_K4) is human immunoglobulin germline segment as shown in the specification (please refer to paragraph [0028] and to Examples 6 and 7 of the specification). The above references are publically available and is known to those skilled in the art and Figures 2a-c and 2b disclose their sequences.

Referring to the attached copy of Immunology 6th edition (Ivan Roitt et al., pages 80-83, Mosby it is well known that light chain genes recombine V and J germline segments to make a gene for the V_L domain and heavy chain genes recombine V, D and J germline segment to make a gene for the V_H domain. Ivan Roitt et al also disclose V_H and J_H gene segments and V_K and J_K gene segments as recombination sequences in immunoglobulin genes. Accordingly, one skilled in the art can easily make heavy chain DP-JH4 and light chain DPK-JK4 with DP as V_H germ line segment and J_H 4 germline segment and DPK as V_K germline segment and J_K4 germline segment using well-known DNA recombinant technique. Since one skilled in the art is already enabled to make heavy chain DP-JH4 and light chain DPK-JK4 as set forth above, it is unnecessary for applicant to include in the specification what is already known in the prior art to satisfy the enablement

requirement of 35 USC 112.

Therefore, applicant is of the opinion that the specification adequately teaches how to make and use the claimed invention and the rejection of claims 6, 7, and 10 for lack of enablement should be withdrawn.

The rejection of claim 2 under 35 USC 102(b) as being anticipated by Leong et al (Cytokine, November 2001, Vol. 16, p 106-119) is respectfully traversed.

The Examiner alleges Leong et al discloses a method of preparing humanized anti IL-8 antibody comprising performing alanine scanning mutagenesis of the murine CDRs, selecting alanine substituted amino acid positions that contribute to the binding to human IL-8, and grafting the alanine substituted CDR regions of the murine anti IL-8 onto the human IgG framework, and this Leong et al discloses the present method of replacing each amino acid residue in the CDR region of murine monoclonal antibody.

Leong et al teaches an anti IL-8 monoclonal antibody which was humanized by grafting the CFR onto the human IgG framework. However, the subsequent alanine scanning mutagenesis and phage display techniques were used only for an affinity maturation of the antibody. Stated otherwise, Leong et al merely discloses the use of subsequent alanine scanning mutagenesis for the affinity maturation of the humanized antibody already constructed by CDR-grafting and that the subsequent alanine scanning mutagenesis was not disclosed for use in a process

for humanizing the antibody. The Examiner alleged that Leong et al discloses the antibody comprising the alanine substituted CDR.

In contrast and in accordance with the present invention, the alanine scanning mutagenesis is used for the determination of specificity in determining the residue (SDR) among CDR in the process for humanizing antibody and not for an affinity maturation of an already humanized antibody.

The CDR of the present invention comprises the amino acid residues which highly involves an antigen biding to the antibody amid CDR. Namely, the amino acid sequences of the SDR are original amino acid sequences of the monoclonal antibody, not alanine substituted sequences. Accordingly, replacing every amino acid of the CFRs of a murine antibody with alanine to determine the SDRs and grafting the SDRs onto the human antibody as taught in the present invention is not disclosed nor suggested in Leong et al.

Accordingly, claim 2 is not anticipated by Leong et al and the rejection under 35 USC 102 should be withdrawn.

The rejection of claim 3 under 35 USC 103(a) as being obvious over Maeng et al (Virology, 2000, Vol. 270, p. 9-16) in view of Leong et al (Cytokine, November 2001, Vol. 16, p. 106-119) is respectfully traversed.

If necessary, applicant will consider the suggestions of the Examiner regarding overcoming the rejection of claim 3 by a showing based upon either paragraph (1) or paragraph (3). However, applicant does not believe that such a showing is necessary in that the present invention is drawn to a process which is not known or obvious from any of the cited references cited taken individually or in combination. The fact that the murine monoclonal antibody KR 127 is taught in Maeng et al and that the heavy chain of SEQ ID NO:2 and a light chain of SEQ ID NO:4 may inherently be present as sequences of the KR 127 antibody is not an inherent teaching of the claimed process. It would not be obvious to one skilled in the art to replace each amino acid residue in the complimentary determining region (CDR) of murine monoclonal antibody heavy and light chain variable regions, to determine from the replaced amino acid residues of the transformant produced by the replacement of each amino acid residue a specificity determining residue (SDR) and to then graft said SDR to at least one of the corresponding amino acid residues into human antibody variable regions. Since claim 3 is a dependent claim, all of the steps in claim 2 from which it depends are claim limitations.

For all of the above reasons, the rejection of claim 3 under 35 USC 103(a) should be withdrawn.

Reconsideration and allowance of claims 2-10 is respectfully solicited.

Respectfully submitted,

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CERTIFICATE OF TRANSMISSION

I hereby certify that this Amendment is being sent to the U.S. Patent Office via EFS-Web to the Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450 on June 18, 2008.

By _____
Audrey de Souza